



**University of  
Zurich**<sup>UZH</sup>

**Zurich Open Repository and  
Archive**

University of Zurich  
University Library  
Strickhofstrasse 39  
CH-8057 Zurich  
[www.zora.uzh.ch](http://www.zora.uzh.ch)

---

Year: 2015

---

## **The association of neurocognitive impairment with diminished expression and apathy in schizophrenia**

Hartmann-Riemer, Matthias N ; Hager, Oliver M ; Kirschner, Matthias ; Bischof, Martin ; Kluge, Agne ; Seifritz, Erich ; Kaiser, Stefan

**Abstract:** Negative symptoms can be grouped into the two dimensions of diminished expression and apathy, which have been shown to be dissociable regarding external validators, such as functional outcome. Here, we investigated whether these two dimensions differentially relate to neurocognitive impairment in schizophrenia. 47 patients with schizophrenia or schizoaffective disorder and 33 healthy control participants were subjected to a neurocognitive test battery assessing multiple cognitive domains (processing speed, working memory, verbal fluency, verbal learning and memory, mental planning), which are integrated into a composite cognition score. Negative symptoms in patients were assessed using the Brief Negative Symptom Scale. We found that diminished expression significantly related to neurocognitive impairment, while severity of apathy symptoms was not directly associated with neurocognition. Other assessed clinical variables include chlorpromazine equivalents, positive symptoms, and depressive symptoms and did not influence the results. Our results are in line with a cognitive resource limitation model of diminished expression in schizophrenia and indicate that cognitive remediation therapy might be helpful to ameliorate expressive deficits.

DOI: <https://doi.org/10.1016/j.schres.2015.10.032>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-120524>

Journal Article

Accepted Version



The following work is licensed under a Creative Commons: Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.

Originally published at:

Hartmann-Riemer, Matthias N; Hager, Oliver M; Kirschner, Matthias; Bischof, Martin; Kluge, Agne; Seifritz, Erich; Kaiser, Stefan (2015). The association of neurocognitive impairment with diminished expression and apathy in schizophrenia. *Schizophrenia Research*, 169(1-3):427-432.

DOI: <https://doi.org/10.1016/j.schres.2015.10.032>

## **The association of neurocognitive impairment with diminished expression and apathy in schizophrenia**

Matthias N. Hartmann-Riemer<sup>a,b,\*</sup>, Oliver M. Hager<sup>a,b</sup>, Matthias Kirschner<sup>a</sup>, Martin Bischof<sup>a</sup>, Agne Kluge<sup>a</sup>, Erich Seifritz<sup>a</sup>, Stefan Kaiser<sup>a</sup>

*<sup>a</sup>Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital, University of Zurich, Zurich, Switzerland.*

*<sup>b</sup>Laboratory for Social and Neural Systems Research, Department of Economics, University of Zurich, Zurich, Switzerland.*

\*Corresponding author. Tel.: +41 44 384 28 17; fax: +41 44 383 44 56. E-mail address: [matthias.hartmann@uzh.ch](mailto:matthias.hartmann@uzh.ch)

**Abstract**

Negative symptoms can be grouped into the two dimensions of diminished expression and apathy, which have been shown to be dissociable regarding external validators, such as functional outcome. Here, we investigated whether these two dimensions differentially relate to neurocognitive impairment in schizophrenia. 47 patients with schizophrenia or schizoaffective disorder and 33 healthy control participants were subjected to a neurocognitive test battery assessing multiple cognitive domains (processing speed, working memory, verbal fluency, verbal learning and memory, mental planning), which are integrated into a composite cognition score. Negative symptoms in patients were assessed using the Brief Negative Symptom Scale. We found that diminished expression significantly related to neurocognitive impairment, while severity of apathy symptoms was not directly associated with neurocognition. Other assessed clinical variables include chlorpromazine equivalents, positive symptoms, and depressive symptoms and did not influence the results. Our results are in line with a cognitive resource limitation model of diminished expression in schizophrenia and indicate that cognitive remediation therapy might be helpful to ameliorate expressive deficits.

*Keywords:* Schizophrenia, Neuropsychology, Amotivation, Flat affect

## 1. Introduction

Schizophrenia is a debilitating disorder characterized by positive symptoms (i.e., delusions and hallucinations), negative symptoms (i.e., blunted affect, alogia, anhedonia, avolition, and asociality) and neurocognitive deficits. While positive symptoms can often be successfully treated with antipsychotic medication, negative symptoms and neurocognitive deficits seem to be more resistant to current treatments (Arango et al., 2004; Keefe et al., 2007). Moreover, neurocognitive deficits and negative symptoms have been linked to poor functional outcome (G. Fervaha et al., 2014; Milev et al., 2005), emphasizing the need for more effective treatment options.

Neurocognitive deficits are a reliable finding in patients with schizophrenia when compared to healthy controls (Fioravanti et al., 2005; Heinrichs and Zakzanis, 1998). The severity of negative symptoms has been reported to correlate with neurocognitive impairment cross-sectionally with weak to moderate effect sizes (Addington et al., 1991; Strauss et al., 2012b). However, there is still a debate about the nature of their relationship (Harvey et al., 2006).

There is now consensus in the field that negative symptoms can be grouped into two separable dimensions (Foussias and Remington, 2010; Messinger et al., 2011). The first dimension, *diminished expression*, comprises symptoms of blunted affect and alogia. The second dimension groups deficits in motivation and pleasure, which manifest themselves as symptoms of anhedonia, avolition, and asociality. We refer to this dimension as *apathy*. Diminished expression and apathy have been shown to differentially relate to functional outcome (Strauss et al., 2013), decision-making (Hartmann et al., 2015), or neural reward processing (Hager et al., 2015; Kirschner et al., 2015), potentially indicating differences in underlying mechanisms. In line with this, studies have investigated the cognitive correlates of diminished expression and apathy separately. Cohen and colleagues proposed a cognitive resource limitation model of diminished expression (Cohen et al., 2012), according to which diminished expression is caused by insufficient cognitive resources that are needed for the complex initiation and adaptation of gestures and facial and vocal expression. There is evidence for this hypothesis in a sample of participants with schizotypal personality (Cohen et al., 2012) and schizophrenia (Chang et al., 2014a; Cohen et al., 2013a). However, an early study by Blanchard and colleagues found no consistent relation of neurocognitive performance with expressive deficits (Blanchard et al., 1994). Moreover, several studies have reported that motivational deficits in schizophrenia were linked to poorer performance on neurocognitive measures (G. Fervaha et al., 2014; Gard et al., 2009; Nakagami et al., 2008;

Roth et al., 2004; Schmand et al., 1994). Recently, studies have investigated correlates of neurocognitive deficits with clinical ratings scales that allow the assessment of both negative symptom dimensions. Ventura et al. (2014) used the Scale for Assessment of Negative Symptoms (SANS; Andreasen, 1982) and reported that both dimensions correlated with neurocognitive deficits. Kring et al. (2013) and Gur et al. (2015) reported no significant correlations using the Clinical Assessment Interview for Negative Symptoms (CAINS; Kring et al., 2013). In a large-scale multicenter study by Galderisi et al. (2014) apathy correlated weakly and diminished expression moderately with neurocognitive deficits using the Brief Negative Symptom Scale (BNSS; Kirkpatrick et al., 2011). In sum, although it is well established that negative symptoms correlate with neurocognitive deficits with weak to moderate effect sizes, findings regarding specific relations with negative symptom dimensions are inconsistent. Given that the correlation between diminished expression and apathy is moderately high (Strauss et al., 2012a), it is thus unclear whether they independently relate to neurocognitive deficits or if one dimension is driving the potential association.

In the current cross-sectional study, we aimed to extend the literature on the relationship between negative symptoms and neurocognition in schizophrenia. More specifically, we aimed to independently assess the relative contribution of diminished expression and apathy (while controlling for variation in the other). Based on the review of the literature, we hypothesized to replicate the link between neurocognitive deficits and overall negative symptoms. Due to the inconsistency in the literature on the association of neurocognitive deficits with the two negative symptom dimensions an exploratory approach was pursued in relation to apathy and diminished expression.

## 2. Methods

### 2.1. Participants

47 patients (SZ) meeting *DSM-IV* criteria for schizophrenia ( $n = 41$ ) or schizoaffective disorder ( $n = 6$ , no mood episode) and 33 healthy control participants (HC) were included in the current study. We decided to include patients with schizoaffective disorder, because we apply a dimensional approach (Barch et al., 2013; Kaiser et al., 2011). Exclusion of the patients with schizoaffective disorder did not change the main results of the paper. Patients were either outpatients ( $n = 20$ ) or post-acute inpatients ( $n = 27$ ) recruited from units of the Psychiatric Hospital of the University of Zurich or affiliated institutions. All patients were clinically stable and all but one unmedicated patient received a stable dose of medication. All medicated patients received atypical antipsychotics and none of the patients received

anticholinergic medication. All inpatients were at the end of their hospitalization and took part in a multimodal treatment program and engaged in activities outside of the hospital, allowing appropriate assessment of negative symptoms. Diagnoses of schizophrenia or schizoaffective disorder were confirmed using the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998). Patients were excluded if (a) criteria for any other *DSM-IV* axis I disorder were met, (b) if daily *lorazepam* dosage exceeded 1 mg, (c) if florid positive symptoms were present, that is, any positive subscale item score of the Positive and Negative Syndrome Scale (Kay et al., 1987) higher than four, or (d) if extrapyramidal symptoms were present on clinical examination. Thus, in line with the NIMH-MATRICES consensus statement on negative symptoms (Kirkpatrick et al., 2006), we defined our exclusion criteria to control for principal sources of secondary negative symptoms (positive symptoms, depression, medication side-effects). There was no inclusion criterion with respect to negative symptom severity, as we aimed to include patients with broad range of symptom severity. HC participants were also screened for neuropsychiatric disorders with the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) to ensure the absence of previous or present neuropsychiatric illness. The present study was approved by the local ethics committee (ethics committee of the canton of Zurich) and written informed consent was obtained from all participants.

## 2.2. Clinical Rating Scales

To assess negative symptoms, we applied the BNSS (Kirkpatrick et al., 2011) in the patient sample. The BNSS was translated to German by the senior author and back-translated by an attending psychiatrist who was BNSS-naïve and native English speaking. Assessment of inter-rater reliability showed an excellent intra-class correlation coefficient (ICC) of .97 for the total score and .87 to .97 for the subscales (anhedonia: .88, asociality: .95, avolition: .87, blunted affect: .95; alogia: .97; Bischof et al., submitted). The diminished expression dimension included the subscales alogia and blunted affect, while the apathy dimension included anhedonia, asociality, and avolition subscales.

Further psychopathological assessment included the PANSS (Kay et al., 1987), the Personal and Social Performance Scale (Schaub and Juckel, 2011), and the Calgary Depression Scale for Schizophrenia (CDSS; Addington, Addington, & Schissel, 1990).

## 2.3. Neuropsychological Assessment

Participants were subjected to a test battery that assessed performance in neurocognitive domains commonly impaired in schizophrenia (processing speed, working

memory, verbal fluency, verbal learning and memory, mental planning) (Heinrichs and Zakzanis, 1998). The test battery included the the following tests: Digit-Symbol Coding and Digit Span of the Wechsler Adult Intelligence Scale Version III (Von Aster et al., 2006), Corsi block-tapping test (Kessels et al., 2000), verbal fluency (Delis et al., 2001), Rey Auditory Verbal Learning Test (Helmstaedter and Durwen, 1990), and the Tower of London (Shallice, 1982). Please note that the applied test battery is not exhaustive in terms of reported neurocognitive deficits in schizophrenia, i.e. there were no tests of motor deficits, visual learning or social cognition.

Five neuropsychological domain scores were calculated from indices of the assessed tests: *processing speed* (Digit-Symbol Coding), *working memory* (mean of Digit Span backwards and Corsi block-tapping test backwards), *verbal fluency* (mean of semantic and phonemic fluency), *verbal learning and memory* (mean of RAVLT total words recalled in all trials and RAVLT delayed recall), *mental planning* (Tower of London). We calculated a *composite cognition* score as the weighted mean of these five neuropsychological domains, which were previously z-transformed based on the data of the HC group.

To control for lack of effort in the neuropsychological assessment, we calculated the Reliable Digit Span (RDS; Greiffenstein et al., 1994) as an embedded performance validity test. The RDS is calculated as the sum of the longest number of digits correctly repeated in the forward and backward condition of the Digit Span test of the Wechsler Adult Intelligence Scale Version III (Von Aster et al., 2006). We applied the conservative cut-off criterion of  $\leq 6$  to avoid false positives.

#### 2.4. Statistical Analyses

Potential group differences in demographic and cognitive measures were assessed using two-sample *t* or Mann-Whitney *U* tests for continuous and chi-square tests for categorical variables. Degrees of freedom were adjusted if Levene's test indicated inequality of variances. Effect sizes of group differences are reported as Cohen's *d*, *r* or Phi coefficient. Bivariate relationships between the two negative symptom dimensions of apathy and diminished expression, the five neuropsychological domains, and the composite cognition score were assessed using Pearson correlation coefficients. To test whether the correlations between the two symptom dimension and neurocognition were significantly different, we applied Steiger's Z-test (Steiger, 1980). Next, we computed partial correlations to independently assess the relationship between each of the two dimensions and performance in the neurocognitive domains while controlling for the other dimension. Additionally,

hierarchical multiple regression was used to evaluate the contribution of diminished expression and apathy in predicting composite cognition. In a first model, apathy was entered first followed by diminished expression, while the second model was computed vice versa. Effect sizes of regression models are reported as Cohen's  $f^2$ .

The current paper reports multiple statistical inferences, which increases the chance of false positives. Considering the exploratory nature of the study, we did not adjust the  $p$ -values for multiple comparisons. All analyses were conducted using SPSS version 22 (IBM Corp.).

### 3. Results

#### 3.1. Sample Characteristics

Demographic and clinical characteristics and cognitive test scores of the SZ and HC group are presented in Table 1. SZ participants performed significantly worse in the cognitive domains of processing speed, verbal fluency, verbal learning and memory, mental planning, and also on the composite cognition score. However, differences in the working memory score did not reach significance.

Three patients failed to pass the performance validity test (RDS; cut-off criterion  $\leq 6$ ) with a value of 6 (6.4% of total patient sample), while none of the control participants failed the criterion. Groups were not significantly different regarding performance validity (Fisher's Exact Test;  $p = .26$ ). Due to the small number of failures, the issue of disentangling lack of effort from motivational negative symptoms, and the fact that exclusion did not change our main conclusion (see 3.2.), we decided to include all patients in further analyses.

#### 3.2. Correlational Analyses

Bivariate Pearson correlations ( $r$ ) between negative symptoms and cognitive test scores are presented in Table 2. Significant correlations with both negative symptom dimensions were found with the domains of verbal fluency and verbal learning and memory. However, the correlations between symptoms and the domains of processing speed, working memory, and mental planning were not significant. Only the dimension diminished expression correlated significantly with the composite cognition score, while the correlation with the apathy dimension did not reach significance. However, according to a Steiger's  $Z$ -test these correlations were not significantly different from each other ( $Z = 1.00$ ,  $p = 0.32$ ).

Although diminished expression and apathy segregate as independent dimensions in factor analytic studies, they co-occur in patients with schizophrenia. In the current study, the correlation was  $r = .44$  ( $p = .002$ ). We applied partial correlations to independently assess the



dimensions relation with the neurocognitive domains and composite cognition (see Table 2 coefficients in brackets). None of the cognitive test indices were related to apathy when variation in severity of diminished expression was held constant. However, when apathy was held constant, diminished expression significantly correlated with verbal learning and memory and mental planning and the composite cognition score.

Other relevant clinical and demographic variables (chlorpromazine [CPZ] equivalents, positive symptoms, depressive symptoms, age) were not significantly associated with composite cognition (all  $r$ 's < .22, all  $p$ 's > .14). The partial correlation between diminished expression symptoms and composite cognition score (controlling for apathy symptoms) remains significant when holding CPZ equivalents, positive symptoms, depressive symptoms, and age constant ( $r = -.41$ ,  $p = .008$ ).

### 3.3. Regression Analyses

Hierarchical multiple regression was used to further investigate the contribution of diminished expression and apathy in predicting composite cognition (Table 3). In the first model, diminished expression predicted 14% of the variance, with apathy accounting for no additional variation in neurocognitive performance (Table 3A). A second model with apathy entering the model first, revealed that apathy explained .5% of the neurocognitive deficits, while diminished expression accounted for an additional 13.5% of the variance (Table 3B). This indicates that the link between negative symptoms and neurocognitive deficits in the present patient sample is mainly driven by variation in expressive deficits.

## 4. Discussion

Here, we investigated whether the two negative symptom dimensions of diminished expression and apathy differentially relate to neurocognitive impairment in schizophrenia. On the level of cognitive subdomains, it was found that verbal fluency and verbal learning and memory were significantly associated with both negative symptom dimensions, while only diminished expression significantly correlated with a composite cognition score. When variation in the other dimension was controlled for, verbal fluency, verbal learning and memory, and mental planning showed significant correlations with diminished expression. However, none of the partial correlations between apathy and neurocognitive domains reached significance. Moreover, when the two symptom dimensions are entered into one regression model, only diminished expression meaningfully predicts neurocognitive deficits. It is important to note that we excluded patients with the principal causes of secondary

negative symptoms – current psychosis, depression and extrapyramidal side-effects. Furthermore, the results were not driven by clinical variables, such as chlorpromazine equivalents, positive symptoms, depressive symptoms or age of the patients. In other words, the observed associations are likely to be driven mainly by primary negative symptoms.

The main finding of the current study, the association of diminished expression with decreased overall cognitive performance, is in line with the cognitive resource limitation theory proposed by Cohen and colleagues (Cohen et al., 2012). This theory states that if cognitive performance is decreased in a psychiatric disorder, such as SZ, fewer resources are available for complex expressive action and interaction. Studies supporting the theory by Cohen et al. in regard to schizophrenia have used a self-report measure (Cohen et al., 2012), a clinician rating scale (Chang et al., 2014b), or a computerized acoustic analysis (Cohen et al., 2013b) to assess symptoms of diminished expression. Recent studies have assessed diminished expression together with apathy in clinical rating scales, reporting mixed results regarding their link to neurocognitive deficits (Galderisi et al., 2014; Gur et al., 2015; Kring et al., 2013; Ventura et al., 2014). Critically, none of these studies investigated the independent relationship of the two negative symptom dimensions with cognitive function. Here, we took this into account and found that dominant role of diminished expression in driving the negative symptom-cognition link.

In partial contrast to our data, studies have suggested that motivational deficits (i.e., apathy) in schizophrenia are linked to cognitive deficits (Gagan Fervaha et al., 2014; Roth et al., 2004), especially to deficits in executive functions (Faerden et al., 2009; Konstantakopoulos et al., 2011). In the present study, the correlation between apathy and composite cognition failed to reach significance. Moreover, apathy did not correlate significantly with tests probing executive functions (working memory and mental planning). These discrepancies might be due the moderate sample size of the present study or differences in applied instruments to assess symptoms and neuropsychological functioning. However, although our data suggest a stronger link of diminished expression with cognition, it is plausible that motivational deficits also impact cognitive performance. Notably, the causal chain linking symptoms and cognition might be crucially different. According to the cognitive resource limitation model, cognitive deficits cause a reduction in expression, while above mentioned studies argue that motivational deficits would cause deficits in cognitive performance. Further research is needed to elucidate these potentially complex interactions.

Ratings on the degree of diminished expression and apathy rely on different sources of information. The clinician makes inferences about apathy (i.e., anhedonia, asociality,

avolition), which are limited by the patient's awareness and ability to accurately communicate. Diminished expression, on the other hand, is rated according to direct observation of the patient's behavior during the interview. The validation of the German version of the BNSS indicated that apathy dimension showed lower inter-rater reliability than diminished expression. Thus, we cannot rule out the possibility that this (less noise in the measurement of diminished expression) might have contributed to the present results.

A few limitations of the present study warrant mention. First, considering the expected moderate effect sizes in the association of negative symptoms with cognitive deficits and the considerable correlation between the two negative symptom dimensions, our findings have to be replicated in larger samples allowing the study of additional moderator variables. Well-powered future studies will also provide more information about whether the two dependent correlations of the negative symptom dimensions with neurocognition are significantly different. In the current study, the statistical test regarding this question did not reach significance. Second, although we used validated cognitive tests to probe the main cognitive domains, future studies should use consensus cognitive test batteries (Nuechterlein et al., 2008) for improved comparability across studies.

In conclusion, our data are in agreement with the cognitive resource limitations model of diminished expression (Cohen et al., 2012). They extend our knowledge about potential mechanisms underlying negative symptoms and have implications for their treatment. In addition to cognitive behavioral therapy to address apathy in schizophrenia, cognitive remediation therapy could be applied to target diminished expression. Until now, cognitive remediation has been found in some but not all studies to improve overall negative symptoms (Dickinson et al., 2010; Sánchez et al., 2014). Our findings clearly suggest that apathy and diminished expression need to be addressed as separate outcomes in order to clarify the effect of cognitive remediation on negative symptoms. Treatment development seems to be especially important considering that diminished expression might affect the successful maintenance of social and romantic interaction, which in turn might establish or worsen symptoms of apathy. Further studies are needed to clarify the neurobiological basis of this symptom-cognition link, and to evaluate potential specific treatment effects of cognitive remediation therapy on diminished expression. Moreover, it would be of interest to investigate whether cognitive deficits in other psychiatric conditions (e.g., depression) also show a link to diminished expression.

## References

- Addington, J., Addington, D., Maticka-Tyndale, E., 1991. Cognitive functioning and positive and negative symptoms in schizophrenia. *Schizophr. Res.* 5, 123–134.
- Andreasen, N.C., 1982. Negative symptoms in schizophrenia. Definition and reliability. *Arch. Gen. Psychiatry* 39, 784–788.
- Arango, C., Buchanan, R.W., Kirkpatrick, B., Carpenter, W.T., 2004. The deficit syndrome in schizophrenia: implications for the treatment of negative symptoms. *Eur. Psychiatry J. Assoc. Eur. Psychiatr.* 19, 21–26. doi:10.1016/j.eurpsy.2003.10.004
- Barch, D.M., Bustillo, J., Gaebel, W., Gur, R., Heckers, S., Malaspina, D., Owen, M.J., Schultz, S., Tandon, R., Tsuang, M., Van Os, J., Carpenter, W., 2013. Logic and justification for dimensional assessment of symptoms and related clinical phenomena in psychosis: relevance to DSM-5. *Schizophr. Res.* 150, 15–20. doi:10.1016/j.schres.2013.04.027
- Bischof, M., Obermann, C., Hartmann-Riemer, M.N., Hager, O.M., Kirschner, M., Kluge, A., Strauss, G.P., Kaiser, S., submitted. The Brief Negative Symptom Scale: Validation of the German Translation and Convergent Validity With Self-rated Anhedonia and Observer-rated Apathy.
- Blanchard, J.J., Kring, A.M., Neale, J.M., 1994. Flat affect in schizophrenia: a test of neuropsychological models. *Schizophr. Bull.* 20, 311–325.
- Chang, W.C., Hui, C.L.M., Chan, S.K.W., Lee, E.H.M., Wong, G.H.Y., Chen, E.Y.H., 2014a. Relationship between diminished expression and cognitive impairment in first-episode schizophrenia: a prospective three-year follow-up study. *Schizophr. Res.* 152, 146–151. doi:10.1016/j.schres.2013.11.027
- Chang, W.C., Hui, C.L.M., Chan, S.K.W., Lee, E.H.M., Wong, G.H.Y., Chen, E.Y.H., 2014b. Relationship between diminished expression and cognitive impairment in first-episode schizophrenia: a prospective three-year follow-up study. *Schizophr. Res.* 152, 146–151. doi:10.1016/j.schres.2013.11.027
- Cohen, A.S., Kim, Y., Najolia, G.M., 2013a. Psychiatric symptom versus neurocognitive correlates of diminished expressivity in schizophrenia and mood disorders. *Schizophr. Res.* 146, 249–253. doi:10.1016/j.schres.2013.02.002
- Cohen, A.S., Kim, Y., Najolia, G.M., 2013b. Psychiatric symptom versus neurocognitive correlates of diminished expressivity in schizophrenia and mood disorders. *Schizophr. Res.* 146, 249–253. doi:10.1016/j.schres.2013.02.002
- Cohen, A.S., Morrison, S.C., Brown, L.A., Minor, K.S., 2012. Towards a cognitive resource limitations model of diminished expression in schizotypy. *J. Abnorm. Psychol.* 121, 109–118. doi:10.1037/a0023599
- Delis, D.C., Kaplan, E., Kramer, J.H., 2001. Delis-Kaplan executive function system (D-KEFS). Psychological Corporation.
- Dickinson, D., Tenhula, W., Morris, S., Brown, C., Peer, J., Spencer, K., Li, L., Gold, J.M., Bellack, A.S., 2010. A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Am. J. Psychiatry* 167, 170–180. doi:10.1176/appi.ajp.2009.09020264
- Faerden, A., Vaskinn, A., Finset, A., Agartz, I., Ann Barrett, E., Friis, S., Simonsen, C., Andreasen, O.A., Melle, I., 2009. Apathy is associated with executive functioning in first episode psychosis. *BMC Psychiatry* 9, 1. doi:10.1186/1471-244X-9-1
- Fervaha, G., Foussias, G., Agid, O., Remington, G., 2014. Impact of primary negative symptoms on functional outcomes in schizophrenia. *Eur. Psychiatry* 29, 449–455. doi:10.1016/j.eurpsy.2014.01.007
- Fervaha, G., Zakzanis, K.K., Foussias, G., Graff-Guerrero, A., Agid, O., Remington, G., 2014. Motivational deficits and cognitive test performance in schizophrenia. *JAMA Psychiatry* 71, 1058–1065. doi:10.1001/jamapsychiatry.2014.1105
- Fioravanti, M., Carlone, O., Vitale, B., Cinti, M.E., Clare, L., 2005. A Meta-Analysis of Cognitive Deficits in Adults with a Diagnosis of Schizophrenia. *Neuropsychol. Rev.* 15, 73–95. doi:10.1007/s11065-005-6254-9
- Foussias, G., Remington, G., 2010. Negative symptoms in schizophrenia: avolition and Occam's razor. *Schizophr. Bull.* 36, 359–369. doi:10.1093/schbul/sbn094
- Galderisi, S., Rossi, A., Rocca, P., Bertolino, A., Mucci, A., Bucci, P., Rucci, P., Gibertoni, D., Aguglia, E., Amore, M., Bellomo, A., Biondi, M., Brugnoli, R., Dell'Osso, L., De Ronchi, D.,

- Di Emidio, G., Di Giannantonio, M., Fagiolini, A., Marchesi, C., Monteleone, P., Oldani, L., Pinna, F., Roncone, R., Sacchetti, E., Santonastaso, P., Siracusano, A., Vita, A., Zeppegno, P., Maj, M., 2014. The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia. *World Psychiatry* 13, 275–287. doi:10.1002/wps.20167
- Gard, D.E., Fisher, M., Garrett, C., Genevsky, A., Vinogradov, S., 2009. Motivation and its relationship to neurocognition, social cognition, and functional outcome in schizophrenia. *Schizophr. Res.* 115, 74–81. doi:10.1016/j.schres.2009.08.015
- Greiffenstein, M.F., John, W., Gola, T., 1994. Validation of malingered amnesia measures with a large clinical sample. *Psychol. Assess.* 6, 218–224. doi:10.1037/1040-3590.6.3.218
- Gur, R.E., March, M., Calkins, M.E., Weittenhiller, L., Wolf, D.H., Turetsky, B.I., Gur, R.C., 2015. Negative symptoms in youths with psychosis spectrum features: Complementary scales in relation to neurocognitive performance and function. *Schizophr. Res.* 166, 322–327. doi:10.1016/j.schres.2015.05.037
- Hager, O.M., Kirschner, M., Bischof, M., Hartmann-Riemer, M.N., Kluge, A., Seifritz, E., Tobler, P.N., Kaiser, S., 2015. Reward-dependent modulation of working memory is associated with negative symptoms in schizophrenia. *Schizophr. Res.* 168, 238–244. doi:10.1016/j.schres.2015.08.024
- Hartmann, M.N., Hager, O.M., Reimann, A.V., Chumbley, J.R., Kirschner, M., Seifritz, E., Tobler, P.N., Kaiser, S., 2015. Apathy but not diminished expression in schizophrenia is associated with discounting of monetary rewards by physical effort. *Schizophr. Bull.* 41, 503–512. doi:10.1093/schbul/sbu102
- Harvey, P.D., Koren, D., Reichenberg, A., Bowie, C.R., 2006. Negative Symptoms and Cognitive Deficits: What Is the Nature of Their Relationship? *Schizophr. Bull.* 32, 250–258. doi:10.1093/schbul/sbj011
- Heinrichs, R.W., Zakzanis, K.K., 1998. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. *Neuropsychology* 12, 426–445.
- Helmstaedter, C., Durwen, H.F., 1990. VLMT: Verbaler Lern- und Merkfähigkeitstest: Ein praktikables und differenziertes Instrumentarium zur Prüfung der verbalen Gedächtnisleistungen. *Schweiz. Arch. Für Neurol. Psychiatr.* 141, 21–30.
- Kaiser, S., Heekeren, K., Simon, J.J., 2011. The negative symptoms of schizophrenia: category or continuum? *Psychopathology* 44, 345–353. doi:10.1159/000325912
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. *Schizophr. Bull.* 13, 261–276. doi:10.1093/schbul/13.2.261
- Keefe, R.S.E., Bilder, R.M., Davis, S.M., Harvey, P.D., Palmer, B.W., Gold, J.M., Meltzer, H.Y., Green, M.F., Capuano, G., Stroup, T.S., McEvoy, J.P., Swartz, M.S., Rosenheck, R.A., Perkins, D.O., Davis, C.E., Hsiao, J.K., Lieberman, J.A., CATIE Investigators, Neurocognitive Working Group, 2007. Neurocognitive effects of antipsychotic medications in patients with chronic schizophrenia in the CATIE Trial. *Arch. Gen. Psychiatry* 64, 633–647. doi:10.1001/archpsyc.64.6.633
- Kessels, R.P., van Zandvoort, M.J., Postma, A., Kappelle, L.J., de Haan, E.H., 2000. The Corsi Block-Tapping Task: standardization and normative data. *Appl. Neuropsychol.* 7, 252–258. doi:10.1207/S15324826AN0704\_8
- Kirkpatrick, B., Fenton, W.S., Carpenter, W.T., Marder, S.R., 2006. The NIMH-MATRICES Consensus Statement on Negative Symptoms. *Schizophr. Bull.* 32, 214–219. doi:10.1093/schbul/sbj053
- Kirkpatrick, B., Strauss, G.P., Nguyen, L., Fischer, B.A., Daniel, D.G., Cienfuegos, A., Marder, S.R., 2011. The Brief Negative Symptom Scale: Psychometric Properties. *Schizophr. Bull.* 37, 300–305. doi:10.1093/schbul/sbq059
- Kirschner, M., Hager, O.M., Bischof, M., Hartmann, M.N., Kluge, A., Seifritz, E., Tobler, P.N., Kaiser, S., 2015. Ventral striatal hypoactivation is associated with apathy but not diminished expression in patients with schizophrenia. *J. Psychiatry Neurosci.* JPN 40, 140383.
- Konstantakopoulos, G., Ploumpidis, D., Oulis, P., Patrikelis, P., Soumani, A., Papadimitriou, G.N., Politis, A.M., 2011. Apathy, cognitive deficits and functional impairment in schizophrenia. *Schizophr. Res.* 133, 193–198. doi:10.1016/j.schres.2011.07.003

- Kring, A.M., Gur, R.E., Blanchard, J.J., Horan, W.P., Reise, S.P., 2013. The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation. *Am. J. Psychiatry* 170, 165–172. doi:10.1176/appi.ajp.2012.12010109
- Messinger, J.W., Trémeau, F., Antonius, D., Mendelsohn, E., Prudent, V., Stanford, A.D., Malaspina, D., 2011. Avolition and expressive deficits capture negative symptom phenomenology: implications for DSM-5 and schizophrenia research. *Clin. Psychol. Rev.* 31, 161–168. doi:10.1016/j.cpr.2010.09.002
- Milev, P., Ho, B.-C., Arndt, S., Andreasen, N.C., 2005. Predictive Values of Neurocognition and Negative Symptoms on Functional Outcome in Schizophrenia: A Longitudinal First-Episode Study With 7-Year Follow-Up. *Am. J. Psychiatry* 162, 495–506. doi:10.1176/appi.ajp.162.3.495
- Nakagami, E., Xie, B., Hoe, M., Brekke, J.S., 2008. Intrinsic motivation, neurocognition and psychosocial functioning in schizophrenia: testing mediator and moderator effects. *Schizophr. Res.* 105, 95–104. doi:10.1016/j.schres.2008.06.015
- Nuechterlein, K.H., Green, M.F., Kern, R.S., Baade, L.E., Barch, D.M., Cohen, J.D., Essock, S., Fenton, W.S., Frese, F.J., Gold, J.M., Goldberg, T., Heaton, R.K., Keefe, R.S.E., Kraemer, H., Mesholam-Gately, R., Seidman, L.J., Stover, E., Weinberger, D.R., Young, A.S., Zalcman, S., Marder, S.R., 2008. The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. *Am. J. Psychiatry* 165, 203–213. doi:10.1176/appi.ajp.2007.07010042
- Roth, R.M., Flashman, L.A., Saykin, A.J., McAllister, T.W., Vidaver, R., 2004. Apathy in schizophrenia: reduced frontal lobe volume and neuropsychological deficits. *Am. J. Psychiatry* 161, 157–159.
- Sánchez, P., Peña, J., Bengoetxea, E., Ojeda, N., Elizagárate, E., Ezcurra, J., Gutiérrez, M., 2014. Improvements in Negative Symptoms and Functional Outcome After a New Generation Cognitive Remediation Program: A Randomized Controlled Trial. *Schizophr. Bull.* 40, 707–715. doi:10.1093/schbul/sbt057
- Schaub, D., Juckel, G., 2011. [PSP Scale: German version of the Personal and Social Performance Scale: valid instrument for the assessment of psychosocial functioning in the treatment of schizophrenia]. *Nervenarzt* 82, 1178–1184. doi:10.1007/s00115-010-3204-4
- Schmand, B., Kuipers, T., Van der Gaag, M., Bosveld, J., Bulthuis, F., Jellema, M., 1994. Cognitive disorders and negative symptoms as correlates of motivational deficits in psychotic patients. *Psychol. Med.* 24, 869–884.
- Shallice, T., 1982. Specific Impairments of Planning. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 298, 199–209. doi:10.1098/rstb.1982.0082
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J. Clin. Psychiatry* 59 Suppl 20, 22–33;quiz 34–57.
- Steiger, J.H., 1980. Tests for comparing elements of a correlation matrix. *Psychol. Bull.* 87, 245–251. doi:10.1037/0033-2909.87.2.245
- Strauss, G.P., Hong, L.E., Gold, J.M., Buchanan, R.W., McMahon, R.P., Keller, W.R., Fischer, B.A., Catalano, L.T., Culbreth, A.J., Carpenter, W.T., Kirkpatrick, B., 2012a. Factor structure of the Brief Negative Symptom Scale. *Schizophr. Res.* 142, 96–98. doi:10.1016/j.schres.2012.09.007
- Strauss, G.P., Horan, W.P., Kirkpatrick, B., Fischer, B.A., Keller, W.R., Miski, P., Buchanan, R.W., Green, M.F., Carpenter Jr., W.T., 2013. Deconstructing negative symptoms of schizophrenia: Avolition–apathy and diminished expression clusters predict clinical presentation and functional outcome. *J. Psychiatr. Res.* 47, 783–790. doi:10.1016/j.jpsychires.2013.01.015
- Strauss, G.P., Keller, W.R., Buchanan, R.W., Gold, J.M., Fischer, B.A., McMahon, R.P., Catalano, L.T., Culbreth, A.J., Carpenter, W.T., Kirkpatrick, B., 2012b. Next-generation negative symptom assessment for clinical trials: Validation of the Brief Negative Symptom Scale. *Schizophr. Res.* 142, 88–92. doi:10.1016/j.schres.2012.10.012
- Ventura, J., Subotnik, K.L., Ered, A., Gretchen-Doorly, D., Helleman, G.S., Vaskinn, A., Nuechterlein, K.H., 2014. The relationship of attitudinal beliefs to negative symptoms, neurocognition, and daily functioning in recent-onset schizophrenia. *Schizophr. Bull.* 40, 1308–1318. doi:10.1093/schbul/sbu002

Von Aster, M., Neubauer, A., Horn, R., 2006. Wechsler Intelligenztest für Erwachsene (WIE).  
Deutschsprachige Bearbeitung und Adaptation des WAIS-III von David Wechsler.  
Frankfurt/Main Ger. Harcourt Test Serv.

**Table 1**

Demographic and clinical characteristics and cognitive test scores.

	Healthy controls ( <i>n</i> = 33)	Patient group ( <i>n</i> = 47)	Test statistic	<i>p</i> -value	Effect size
<i>Demographics</i>					
Age (years)	33.01 (9.64)	31.30 (7.71)	<i>t</i> = 0.92	.36	<i>d</i> = .21
Gender (male/female)	22/11	34/13	$\chi^2 = 0.30$	.59	Phi = .06
Handedness (r/l)	29/4	43/4	$\chi^2 = 0.28$	.60	Phi = -.06
Education (years) <sup>a</sup>	12.53 (3.30)	11.29 (2.74)	<i>U</i> = 606.00	.09	<i>r</i> = .19
<i>Clinical variables</i>					
CPZ equivalents	-	566.29 (428.88)	-	-	-
Duration of illness (years)	-	8.89 (6.69)	-	-	-
Apathy (BNSS <sup>b</sup> )	-	16.15 (8.42)	-	-	-
Diminished expression (BNSS <sup>b</sup> )	-	9.49 (7.26)	-	-	-
PANSS positive <sup>c</sup>	-	7.17 (2.90)	-	-	-
PANSS negative <sup>c</sup>	-	14.30 (5.93)	-	-	-
PSP scale	-	54.87 (11.39)	-	-	-
CDSS	-	1.91 (2.28)	-	-	-
<i>Cognitive test scores</i>					
Processing speed	0 (1)	-1.08 (.94)	<i>t</i> = 4.92	< .001	<i>d</i> = 1.12
Working memory	0 (1)	-.35 (1.45)	<i>U</i> = 656.50	.24	<i>r</i> = .13
Verbal fluency	0 (1)	-1.00 (.99)	<i>t</i> = 4.39	< .001	<i>d</i> = 1.00
Verbal learning and memory	0 (1)	-1.03 (1.26)	<i>t</i> = 3.92	< .001	<i>d</i> = .89
Mental planning	0 (1)	-.44 (.94)	<i>U</i> = 572.50	.04	<i>r</i> = .23
Composite cognition score	0 (1)	-1.24 (1.28)	<i>t</i> = 4.84	< .001	<i>d</i> = 1.10

*Note.* Data are presented as means and standard deviations. BNSS = Brief Negative Symptom Scale; CDSS = Calgary Depression Scale for Schizophrenia; CPZ = Chlorpromazine; PANSS = Positive and Negative Syndrome Scale; PSP = Personal and Social Performance. <sup>a</sup> Compulsory education in Switzerland is 9 years. <sup>b</sup> *Apathy*: sum of anhedonia, asociality, and avolition; *diminished expression*: sum of blunted affect and alogia. <sup>c</sup> *Positive factor*: P1, P3, P5, G9; *negative factor*: N1, N2, N3, N4, N6, G7.



**Table 2**

Correlation coefficients between the negative symptom dimensions diminished expression and apathy and cognitive test scores in the patient group (n = 47).

	Diminished expression (BNSS)	Apathy (BNSS)
Processing speed	-.09 (-.02)	-.20 (-.19)
Working memory	-.28 (-.25)	-.08 (.06)
Verbal fluency	-.33* (-.21)	-.38* (-.27)
Verbal learning and memory	-.42** (-.33*)	-.32* (-.17)
Mental planning	-.25 (-.36*)	.14 (.28)
Composite cognition score	-.37* (-.31*)	-.22 (-.07)

*Note.* Values are Pearson correlations and partial correlations in brackets (each symptom dimension controlled for the other one). BNSS = Brief Negative Symptoms Scale.

\*  $p < .05$ , \*\*  $p < 0.01$

**Table 3**

Predictors of the composite cognition score in stepwise hierarchical multiple regression.

<b>A</b>	$R^2$	$f^2$	<i>Beta</i>	<i>p</i>
Step 1				
Diminished Expression	.14	.16	-.37	.01
Step 2				
Diminished Expression	.14 <sup>a</sup>	.16 <sup>a</sup>	-.34	.04
Apathy		.0 <sup>b</sup>	-.07	.65
<b>B</b>	$R^2$	$f^2$	<i>Beta</i>	<i>p</i>
Step 1				
Apathy	.05	.05	-.22	.14
Step 2				
Apathy	.14 <sup>a</sup>	.16 <sup>a</sup>	-.07	.65
Diminished Expression		.10 <sup>b</sup>	-.34	.04

*Note.* BNSS = Brief Negative Symptoms Scale. <sup>a</sup>Values relate to the whole model in step 2. <sup>b</sup>Effect size attributable to the addition of second variable to the model.